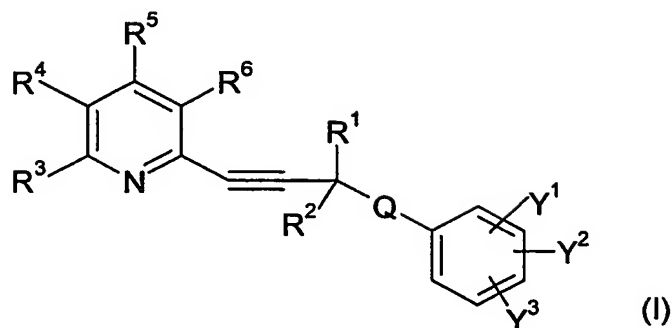


Claims

1. A compound of formula I



wherein

R^1 is selected from hydrogen, C_1 - C_4 alkyl, C_3 - C_6 cycloalkyl, aryl and heteroaryl,
 10 wherein the aryl or heteroaryl may be substituted by C_1 - C_4 alkyl;

R^2 is selected from hydrogen and C_1 - C_4 alkyl;

R^3 is selected from hydrogen, C_1 - C_4 alkyl, F, CF_3 , CHF_2 and CH_2F ;

R^4 is selected from hydrogen, F, CF_3 , CHF_2 , CH_2F and CH_3 ;

R^5 is selected from hydrogen and F;

15 R^6 is selected from hydrogen and F;

Q is selected from C_1 - C_4 alkyl, optionally substituted by C_1 - C_4 alkyl or C_1 - C_4 alkoxy;

Y^1 is selected from hydrogen; halogen; nitrile; C_1 - C_4 alkoxy; C_1 - C_4 alkyl wherein
 one or more of the hydrogen atoms of the alkyl group may be substituted for a
 20 fluorine atom; benzyloxy; nitro in the meta or para position; and C_1 - C_4 alkyl ester;

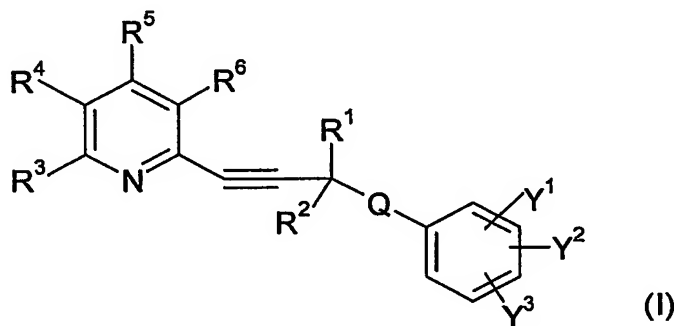
Y^2 is selected from hydrogen; halogen; nitrile; C_1 - C_4 alkoxy; C_1 - C_4 alkyl wherein
 one or more of the hydrogen atoms of the alkyl group may be substituted for a
 fluorine atom; and C_1 - C_4 alkyl ester;

Y^3 is selected from hydrogen; halogen; nitrile; C_1 - C_4 alkoxy; C_1 - C_4 alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and C_1 - C_4 alkyl ester; or

Y^1 and Y^2 may form an aromatic or non-aromatic ring, optionally substituted by halogen, nitrile, C_1 - C_4 alkoxy, C_1 - C_4 alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or C_1 - C_4 alkyl ester;

as well as pharmaceutically acceptable salts, hydrates, isoforms and/or optical isomers thereof, with the exception of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile.

2. A compound of formula I



wherein

R^1 is selected from hydrogen, C_1 - C_4 alkyl, C_3 - C_6 cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by C_1 - C_4 alkyl;

R^2 is selected from hydrogen and C_1 - C_4 alkyl;

R^3 is selected from hydrogen, C_1 - C_4 alkyl, F, CF_3 , CHF_2 and CH_2F ;

R^4 is selected from hydrogen, F, CF_3 , CHF_2 , CH_2F and CH_3 ;

R^5 is selected from hydrogen and F;

R^6 is selected from hydrogen and F;

Q is selected from C_1 - C_4 alkyl, optionally substituted by C_1 - C_4 alkyl or C_1 - C_4 alkoxy;

Y¹ is selected from hydrogen, halogen, nitrile, C₁-C₄ alkoxy, and C₁-C₄ alkyl;
Y² is selected from hydrogen, halogen, nitrile, C₁-C₄ alkoxy, and C₁-C₄ alkyl;
Y³ is selected from hydrogen, halogen, nitrile, C₁-C₄ alkoxy, and C₁-C₄ alkyl;
as well as pharmaceutically acceptable salts, hydrates, isoforms and/or optical
isomers thereof, with the exception of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile.

3. A compound according to formula I of claim 1 or 2, wherein

R¹ is hydrogen or C₁-C₃ alkyl;

R² is hydrogen;

R³ is selected from hydrogen and methyl;

R⁴ is hydrogen;

R⁵ is hydrogen;

R⁶ is hydrogen;

Q is C₁-C₂ alkyl, optionally substituted by C₁-C₂ alkyl;

Y¹ is selected from hydrogen, chloro, C₁-C₂ alkoxy, and C₁-C₂ alkyl; and

Y² is selected from hydrogen, chloro, C₁-C₂ alkoxy, and C₁-C₂ alkyl; and

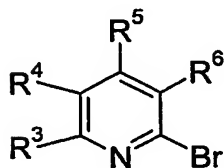
Y³ is hydrogen.

4. A compound according to claim 1 selected from 2-[4-(3-chlorophenyl)but-1-yn-1-yl]-6-methylpyridine, 2-[4-(3-methoxyphenyl)but-1-yn-1-yl]-6-methylpyridine, 2-methyl-6-[4-(3-methylphenyl)but-1-yn-1-yl]pyridine, 2-methyl-6-(4-phenylbut-1-yn-1-yl)pyridine and 2-methyl-6-(4-phenylpent-1-yn-1-yl)pyridine.

5. A compound according to any one of claims 1-4 for use in therapy.

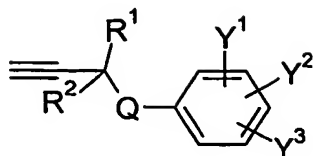
6. A compound according to claim 5, wherein the therapy is treatment or prevention of gastroesophageal reflux disease.

7. Use of a compound according to formula I of claim 1 or 2, or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for the inhibition of transient lower esophageal sphincter relaxations.
- 5 8. Use of a compound according to formula I of claim 1 or 2, or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for treatment or prevention of gastroesophageal reflux disease.
- 10 9. Use of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for the inhibition of transient lower esophageal sphincter relaxations.
- 15 10. Use of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for treatment or prevention of gastroesophageal reflux disease.
- 20 11. A pharmaceutical composition comprising a compound of formula I of claim 1 or 2 as an active ingredient, together with a pharmacologically and pharmaceutically acceptable carrier.
12. A process for the preparation of a compound of formula I, whereby a coupling reaction of an aryl bromide A



A

25 and an alkyne B



B

is performed in the presence of a base such as triethyl amine at room temperature to 60 °C, and wherein

R¹ is selected from hydrogen, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, aryl and heteroaryl,
 5 wherein the aryl or heteroaryl may be substituted by C₁-C₄ alkyl;

R² is selected from hydrogen and C₁-C₄ alkyl;

R³ is selected from hydrogen, C₁-C₄ alkyl, F, CF₃, CHF₂ and CH₂F;

R⁴ is selected from hydrogen, F, CF₃, CHF₂, CH₂F and CH₃;

R⁵ is selected from hydrogen and F;

10 R⁶ is selected from hydrogen and F;

Q is selected from C₁-C₄ alkyl, optionally substituted by C₁-C₄ alkyl or C₁-C₄ alkoxy;

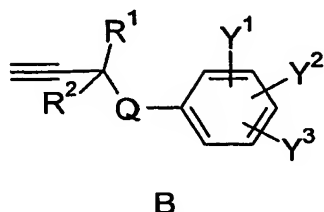
Y¹ is selected from hydrogen; halogen; nitrile; C₁-C₄ alkoxy; C₁-C₄ alkyl wherein
 one or more of the hydrogen atoms of the alkyl group may be substituted for a
 15 fluorine atom; benzyloxy; nitro in the meta or para position; and C₁-C₄ alkyl ester;

Y² is selected from hydrogen; halogen; nitrile; C₁-C₄ alkoxy; C₁-C₄ alkyl wherein
 one or more of the hydrogen atoms of the alkyl group may be substituted for a
 fluorine atom; and C₁-C₄ alkyl ester;

Y³ is selected from hydrogen; halogen; nitrile; C₁-C₄ alkoxy; C₁-C₄ alkyl wherein
 20 one or more of the hydrogen atoms of the alkyl group may be substituted for a
 fluorine atom; and C₁-C₄ alkyl ester; or

Y¹ and Y² may form an aromatic or non-aromatic ring, optionally substituted by
 halogen, nitrile, C₁-C₄ alkoxy, C₁-C₄ alkyl wherein one or more of the hydrogen
 atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or C₁-C₄
 25 alkyl ester.

13. A compound of formula B



wherein

R^1 is selected from hydrogen, C_1 - C_4 alkyl, C_3 - C_6 cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by C_1 - C_4 alkyl;

R^2 is selected from hydrogen and C_1 - C_4 alkyl;

R^3 is selected from hydrogen, C_1 - C_4 alkyl, F, CF_3 , CHF_2 and CH_2F ;

R^4 is selected from hydrogen, F, CF_3 , CHF_2 , CH_2F and CH_3 ;

Q is selected from C_1 - C_4 alkyl, optionally substituted by C_1 - C_4 alkyl or C_1 - C_4 alkoxy;

Y^1 is selected from hydrogen; halogen; nitrile; C_1 - C_4 alkoxy; C_1 - C_4 alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; benzyloxy; nitro in the meta or para position; and C_1 - C_4 alkyl ester;

Y^2 is selected from hydrogen; halogen; nitrile; C_1 - C_4 alkoxy; C_1 - C_4 alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and C_1 - C_4 alkyl ester;

Y^3 is selected from hydrogen; halogen; nitrile; C_1 - C_4 alkoxy; C_1 - C_4 alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and C_1 - C_4 alkyl ester; or

Y^1 and Y^2 may form an aromatic or non-aromatic ring, optionally substituted by halogen, nitrile, C_1 - C_4 alkoxy, C_1 - C_4 alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or C_1 - C_4 alkyl ester.

14. A compound selected from 1-chloro-3-(4,4-dibromobut-3-en-1-yl)benzene; 1-methoxy-3-(4,4-dibromobut-3-en-1-yl)benzene; 1-methyl-3-(4,4-dibromobut-3-en-

1-yl)benzene; 1-but-3-yn-1-yl-3-chlorobenzene; and (4,4-Dibromo-1-methyl-but-3-enyl)-benzene.

15. A method for the inhibition of transient lower esophageal sphincter relaxations
5 whereby an effective amount of a compound of formula I of claim 1 or 2 is
administered to a subject in need of such inhibition.

16. A method for the treatment or prevention of gastroesophageal reflux disease,
10 whereby an effective amount of a compound of formula I or claim 1 or 2 is
administered to a subject in need of such treatment or prevention.